ESC European Society of Cardiology

Europace (2021) **23**, iv11–iv19
doi:10.1093/europace/euab071

SUPPLEMENT PAPER

Prevention of cardiac implantable electronic device infections: guidelines and conventional prophylaxis

Carina Blomstrom-Lundqvist * and Bozena Ostrowska

Department of Medical Sciences, Uppsala University, Uppsala, Sweden

Received 20 January 2021; editorial decision 6 March 2021; accepted after revision 9 March 2021

Abstract Cardiac implantable electronic devices (CIED) are potentially life-saving treatments for several cardiac conditions, but are not without risk. Despite dissemination of recommended strategies for prevention of device infections, such as administration of antibiotics before implantation, infection rates continue to rise resulting in escalating health care costs. New trials conveying important steps for better prevention of device infection and an EHRA consensus paper were recently published. This document will review the role of various preventive measures for CIED infection, emphasizing the importance of adhering to published recommendations. The document aims to provide guidance on how to prevent CIED infections in clinical practice by considering modifiable and non-modifiable risk factors that may be present pre-, peri-, and/or post-procedure.

Keywords CIED • Pacemaker • Defibrillator • Infection • Endocarditis • Risk

Introduction

Infection remains one of the most serious complications of CIED implantations leading to substantial morbidity, hospitalizations, and mortality with associated health-care costs.[1–6] Expanding indications and use of more complex systems, such as CRTs are suggested explanations for the increasing infections rates even outweighing the rise in device implantations.[1,7–10] The observation that complication and infection rates are higher for re-interventions than for *de novo* implantations,[9,11–16] further underlines that primary prevention of infection is particularly important for CRTs and other complex multi-lead procedures and reoperations.

Despite publications of several practice guidelines and consensus documents on prevention and management of CIED infection[17–20] along with multiple attempts to improve their dissemination and implementation, major gaps in knowledge and insufficient adherence to guidelines still remain a challenge as evident in a recent worldwide survey on CIED infection.[21] Major gaps in physicians' knowledge and skills across all stages of CIED care were also identified in a recent EHRA survey.[22] The finding of physicians' lack of confidence and certain system barriers (mainly logistic and attitudinal) for correct referral, may also limit adequate prevention measures of device infections.

Given this background and the knowledge that device complications are common and device infections require complete system removal[23] both generating substantial healthcare costs,[24] novel strategies for the prevention of CIED infection are urgently needed. This section gives an overview of recommended strategies for preventing CIED infections in line with recent EHRA international consensus document on how to prevent, diagnose, and treat CIED infections.[20] Check lists on actionable risk factors and subsequent actions for preventing CIED infections are presented.

Prevention

Prevention of CIED infection encompasses risk evaluation and efforts to avoid complications at several steps in good time before, during, and after the implantation procedure, as outlined in the published

* Corresponding author. Tel: +46186113113. *E-mail address*: carina.blomstrom.lundqvist@akademiska.se

EHRA international consensus document on how to prevent, diagnose and treat Cardiac Implantable Electronic Device infections.[20] Risk stratification for device infection is important because it increases awareness of risk factors that can be eliminated or minimized by various preventive actions at various levels. Many known risk factors for CIED infection can be *modified* and are thus amenable to preventive actions for risk reduction.[9,14,16] An example of such actionable risk factor is the presence of a temporary pacing lead at the time of the implant procedure, which often can be avoided or replaced by other techniques. Although many risk factors *cannot be modified,* particularly those related to certain comorbidities, some of them can be targeted for optimized therapy or minimized by using alternative approaches. An example is diabetes, which albeit being non- modifiable, can be optimally treated prior surgery to lower the risk.[25] Another strong non-actionable risk factor is end-stage renal disease, which cannot per se be modified, but by using alternative techniques or devices, such as a leadless- or subcutaneous system, the risk for infection may be substantially reduced.

Seasonal variations in pocket infections associated with elevated temperatures and precipitation were reported for subgroups including women, elderly people (>75 years), late CIED infection, and skin commensal bacterial infections.[26] Specific prevention strategy should be discussed in these high-risk patients.

Risk factors and preventive actions for CIED infections may further be categorized as patient-, procedure-, or device-related factors. Environmental-, organizational-, and staff-related risk factors can in general be subject to standardized preventive measures, such as facility barriers, quality of environmental cleaning, and access to dedicated operating rooms. A checklist of risk factors for device infection and recommended actions is shown in *Table 1*.

Pre-procedural actions

Mechanisms of infection—preventing contamination

The most common mechanism of CIED infection is local contamination of leads, pulse generator, or pocket during the implantation procedure when crossing the skin barrier.[27] Contamination may occur by introducing the patient's normal skin flora into the wound at the time of skin incision, via the air in the operating room (both host and staff) prior to implantation or via the hands of those implanting or assisting the procedure. Subsequent bacterial colonization results in pocket infection, which then spreads along the leads and cause secondary blood stream infection with progress to systemic infection and endocarditis.[4,28] Staphylococcus species, which are far more prone to adhere to non-biological material than other species, cause nearly 70% of device infections.[29] Device-related infections after initial implant occur earlier, more aggressively, and are often due to *Staphylococcus aureus*, while those after reoperations have more indolent manifestations and are due to coagulase negative staphylococci.[30] The second less common mechanism is haematogenous spread from a distant focal infection with secondary involvement of the CIED system.[31] Gram-negative pathogens and other microbes are found in <10% of cases.[4,31]

Patient selection

Whether the benefit of the device implantation outweighs the risks should always be carefully considered on an individual basis in good time before the procedure. Up to 50% of patients undergoing device removal for infection may not require device re-implantation.[32] The timing and indication for a particular device should be meticulously chosen in order to minimize risk of infection. It is preferable to postpone an implantation and give time for preventive measure rather than neglecting an increased risk for infection that could have been prevented. Alternatives to conventional transvenous systems for high-risk patients are described below.

Patient risk factors for device infection

A thorough clinical history carefully identifying the *presence of comorbidities* as risk factors for infection and corresponding possible preventive actions to reduce the risk is of paramount importance (*Table 1*). Particularly end-stage renal disease and a history of previous device infection have consistently been associated with the highest risks, emphasizing the importance of a careful evaluation whether CIED therapy is absolutely indicated in these patients and which measures can be undertaken to minimize the risk (*Table 1*).[7,11,15,33] Optimized treatment of various conditions may lower the risk for infection, as shown with better glycaemic control in the peri-procedural period in surgical patients with diabetes.[25]

A procedure should always be postponed until a patient has been afebrile for at least 24 h since *pre-procedural fever* has been associated with a higher risk for device-related infection (adjusted OR: 4.8).[12,15] The importance of isolated leucocytosis for device infection is, however, less clear according to a recent study showing no significant association between device infections and preoperative isolated leucocytosis in the absence of other infectious markers, such as bacteraemia, fever, or physical examination suggesting an ongoing infectious process.[34]

Temporary transvenous pacing is associated with a two-fold increased risk for device infections and should therefore be avoided and alternatives sought for (backup transthoracic pacing or infusion of rate-accelerating drugs) if possible (*Table 1*).[12] Temporary pacing via a jugular route may confer a lower risk of infection than access via the groin. Removal of all central venous lines, a well-recognized risk factor for infection, should always be considered before device surgery (*Table 1*).[15]

Choice of alternative device system in high-risk patients

'Leadless' pacemakers may be less prone to infection and can be used in high-risk patients.[35,36] The absence of a pacemaker pocket and transvenous lead may theoretically reduce the risk of device infection although bloodstream seeding of the device by a remote-site infection may still be possible. Whether leadless pacing technology reduces the long-term risks of CIED infection remains to be proven. Subcutaneous ICD (S-ICD) is an option in patients requiring sudden death protection.[37,38] Implanting an epicardial system may be an alternative in high-risk patients.[39]

Medications

The patient's medication, particularly corticosteroids and antithrombotic drugs, may confer an increased risk for infection.[15]

Anticoagulation and antiplatelet drugs. Since clinically significant pocket haematoma, defined as requiring reoperation or interruption of OAC, is associated with >seven-fold increased risk for subsequent

Table 1 Check list of actionable risk factors for prevention of CIED infections

Actionable risk factor	Actions to prevent device infection
Pre-operative actions	
• Comorbidities? • Renal insufficiency • Chronic skin disease • COPD • Diabetes • Heart failure	Optimize medical treatments prior implant: • consider device alternatives • check for skin infections—wounds • optimize respiratory medication • better glycaemic control • optimize heart failure treatment
• Fever/systemic infection?	Postpone procedure until afebrile for ≥24 h or values normalized. Check dental status
• Central venous line? • Temporary transvenous pacing?	• Remove indwelling lines. • Avoid or consider pacing alternatives (isoproterenol, transthoracic pacing, change port)
• Anticoagulation therapy?	• Do not use heparin bridging • Continue or interrupt temporarily if possible
• Antiplatelets?	• Discontinue 5-10 d prior surgery (particularly P2Y12 inhibitors) & avoid DAPT if possible
• Steroid treatment?	• Is withdrawal or dose reduction possible?
• Is procedure complex/expected to be lengthy?	• Consider experienced operator and/or supervisor to shorten procedure time or consider referral to experienced operator/high volume centre
• CIED replacement? • Upgrade to more complex CIED? • Early re-intervention?	• Re-evaluate indication for replacement/upgrade. • Does the benefit of device implantation outweigh the risks? • Consider alternative approach to transvenous system. • Postpone procedure if possible
• Presence of many leads and/or abandoned leads?	• Consider extraction on individual basis
• High-risk patient for infection?	• Consider LPM, S-ICDs or epicardial system if appropriate. • Reconsider indication for device implant • Consider experienced operator or refer to high volume centre if complex procedure
• *S. aureus* colonization	• -Consider nasal swabs and nasal treatment with mupirocin and chlorhexidine skin washing in selected patients
• Is i.v. antibiotic therapy given?	• i.v. flucloxacillin (1–2 g) or cefazolin (1–2 g) within 1 h prior to surgery
• Is procedure scheduled as 'out-of-hours' procedure?	• Postpone procedure to be performed during office hours
Intra-operative actions	
• High-risk patient for infection?	• Consider antibiotic-impregnated mesh envelope (minocycline/rifampicin) • Ensure short procedure times and low complication rate by selecting experienced operators and well-trained staff
• High risk for peroperative haematoma (antithrombotic therapy)?	• Consider pressure dressings • Consider pulsed electron avalanche knife instead of traditional electrocautery • Avoid sub-pectoral pocket unless strongly indicated
• Re-operation?	• Avoid capsulectomy at re-interventions
• Has staff and operating theatre conditions been checked/prepared?	• Restrict number- and exchanges of personnel during procedures • Proper ventilation system, air-quality optimization, • Temperature control
Post-operative actions	
• Is there a high wound dehiscence risk due to haematoma?	Consider surgical pocket evacuation

Reduce risk for pocket haematoma

CIED, cardiac implantable electrical device; COPD, chronic obstructive pulmonary disease; DAPT, dual antiplatelet therapy; i.v., intravenous; LPM, leadless pacemaker; S-ICD, subcutaneous ICD; *S. aureus, Staphylococcus aureus.*

device infection over 1-year follow-up[40] every attempt should be made to avoid such complication. Surgery performed with continued perioperative warfarin vs. interruption with heparin bridging results in 80% fewer clinically significant pocket haematomas (3.5% vs. 16%).[41] Continued vs. interrupted direct oral anticoagulants have similar low risks of pocket haematoma (2.1% in both groups)[42] and direct oral anticoagulants vs. continued warfarin do not seem to differ either while concomitant antiplatelet use doubles that risk.[43]

Given this knowledge, a 'bridging' approach with heparin should not be used during surgery for CIEDs (*Table 1*).[20,41,44,45] Withholding anticoagulation for the procedure and restarting when the bleeding risk is reduced seems reasonable in patients with low risk for stroke, while continuing oral anticoagulants is recommended in higher risk patients (prior embolic event or mechanical valve).[20]

Since antiplatelet therapy doubles the risk of pocket haematoma during device surgery, particularly P2Y12 inhibitors (clopidogrel, prasugrel, and ticagrelor), they should preferably be discontinued for 5–10 days before the surgical intervention.[20,43,46]

Long-term steroid therapy suppressing immunity and delaying wound healing has been associated with device-related infection but is often difficult to withdraw as it usually implies the presence of another coexisting disease, such as chronic obstructive pulmonary disease and rheumatologic diseases.[7,15,30] Conditions that compromise the patient's immune status, which often necessitate steroid use, and malnutrition are also strong risk factors for CIED infection.[7]

Leads

The decision to abandon or extract a lead must be made on an individual basis weighing all known risks and benefits.[47,48] There is a greater risk of infection with increasing number of implanted leads and if abandoned leads are present.[49,50]

Staphylococcus aureus decolonization of patients

Nasal swabs can detect *S. aureus* colonization by means of a real-time polymerase chain reaction (PCR) assay in patients scheduled for elective procedures. Nasal treatment with mupirocin and chlorhexidine skin washing has been shown to reduce the risk of hospital-associated *S. aureus* infection from 7.7% in placebo groups to 3.4%.[51]

Pre-procedure skin preparation

Data are diverse regarding benefits of routine pre-surgical washing with an anti-microbial agent.[52] Studies on preoperative chlorhexidine skin preparation indicate a reduced risk for infection in patients undergoing knee and hip arthroplasty though.[53] Electronic clippers with a single-use head (not razors) should be used if chest hair removal is required (*Table 2*).[54]

Pre-procedure antibiotic prophylaxis

Prophylactic intravenous antibiotic therapy is standard-of-care for prevention of CIED infection, based on randomized controlled trials and meta-analysis showing 70% relative risk reduction in device-related infections.[54,55] The lack of preoperative antibiotics prophylaxis is the strongest predictor of CIED infection.[15] Prophylactic systemic antibiotics covering at least *S. aureus* species,[55] including i.v. flucloxacillin (1–2 g) and first-generation cephalosporins, such as cefazolin (1–2 g), is recommended based on randomized trials[54–56] and must be completed within 1 h of incision to ensure adequate tissue levels. In case of allergy to cephalosporins, vancomycin (15 mg/kg) may be used and administered slowly over 1 h starting 90–120 min prior to the incision. Routine methicillin-resistant *S. aureus* (MRSA) coverage should be guided by the prevalence of MRSA in the implanting institution and patient risk. Repeat dosing of antimicrobials is not recommended after skin closure.

Re-intervention, upgrade, and replacement

Every effort should be made to avoid procedure-related complications, particularly re-intervention for lead dislodgement, which increases the risk for infection by sixth-fold.[9,15,57] Since generator change is associated with a roughly two-fold risk for infection, the decision to replace a device should be made by weighing benefits and risks for device-related infection and death.

The timing of re-intervention is important and seems to correlate with the risk of CIED infections. Early re-interventions, defined as repeat procedures performed within the index admission period prior to discharge, dramatically increases the risk of CIED infection with >15-fold increased risk.[12] All measures must therefore be taken to avoid an early re-intervention. Whether a strategy of postponing a re-intervention by weeks (e.g. for lead repositioning) can effectively reduce the risk of infection is unclear though and requires further research.

Risk stratification for prevention

Several studies developing risk scores to predict patients at higher pre-procedural risk of device infection have mainly aimed to identify those who would benefit from antibacterial envelope.[56,58–60] Such *risk stratification* score may better identify patients at risk than individual factors, but further validation is warranted in independent prospective cohorts (see specific section below). The PADIT risk score, aiming to identify higher risk patients that can benefit from targeted interventions to reduce the risk of CIED infection, may provide additional predictive value, particularly if prior CIED infection is considered.[61]

Pre-procedure-related preventive actions for high-risk patients are described in *Tables 1 and 2*.

Intra-operative actions

Surgical skin preparation

Pre-operative antiseptic skin cleansing aims to eliminate colonizing bacteria on the skin. The optimal choice of topical antiseptic is unclear since no randomized data exist for CIED implantation procedures. Alcoholic 2% chlorhexidine was superior to povidone-iodine for skin preparation in one randomized trial prior to surgery[62] or intra-vascular catheter insertion[63] and is therefore recommended (*Table 2*).[20] A single-centre retrospective cohort study of patients receiving a CIED failed to observe a difference in infection rates between these topical antiseptics, but the infection rate was small.[64] The antiseptic should be left until dried completely before incision to give sufficient time for it to be effective. There are no data suggesting that iodine-impregnated adhesive incise drapes reduce infection rates.[65]

Double-gloving

Table 2 Recommended actions for prevention of device infections according to EHRA consensus document

Consensus statement	Scientific evidence coding
Pre-procedural actions	
Confirm indication for CIED	E
Delay CIED implantation in patients with infection	E
Avoid temporary transvenous pacing and central venous lines, which should ideally be removed prior to introducing new hardware, whenever possible	O, M
Measures to avoid pocket haematoma are recommended (avoid heparin bridging, discontinue antiplatelets if possible)	R
Periprocedural use of therapeutic Low-molecular-weight-heparin	R, M, O
Perform the CIED procedure in an operating room/suite with complete sterile environment as required for other surgical implant procedures.	E
Procedure should be performed or supervised by an operator with sufficient training and experience	O
• Operators with ∼<100 CIED procedures experience should work under close supervision of more experienced operators	O, E
• An annual minimum operator volume of ∼50 CIED procedures is recommended for all operators	
Topical *S. aureus* decolonization may be performed	E
Pre-procedural skin wash may be performed	E
Hair removal with electric clippers (not razors) is recommended	O
Antibiotic prophylaxis is recommended within 1 h of incision for cefazolin and flucloxacilline, within 90–120 min for vancomycin	R, M
A continuous surveillance program of infection rates and associated microbiology should be set-up at the level of each implanting centre	E
Intra-procedural actions	
Surgical preparation with alcoholic chlorhexidine should be used rather than povidone-iodine	R
Allow sufficient time for the antiseptic preparation to dry	E
Adhesive iodophor-impregnated incise drapes may be used	E
Perform the procedure with adequate surgical technique—minimize tissue damage, haemostasis, adequate wound closure	E
Antibiotic envelope in high-risk situations is recommended*	R
If the operator performs the prepping and draping, glove change/re-scrub or remove outer glove of a double-glove before incision	E
Using local instillation of antiseptic and antibiotics in the pocket	R, E
Use of braided sutures for final skin closure	E
Post-procedural actions	
Use of post-operative antibiotic therapy	R
Adequate dressing for 2–10 days is recommended	E
Patient instructions on wound care should be provided	E
Delay or reconsider indication for re-intervention if possible	E
Haematoma drainage or evacuation (unless tense, wound dehiscence is present or pain is severe)	O
Prevention of infections related to device implantations in elderly, paediatric patients and in adults with congenital heart disease	
Implanting physicians should be aware of the higher CIED infection risks in frail and elderly patients. Submuscular position of PM or ICD generators is recommended in selected elderly patients with limited subcutaneous tissue to prevent device erosion.	O
Implanting physicians should be skilled in multiple and alternative surgical approaches performed in paediatric, congenital heart disease, and ACHD patients related to a higher risk of CIED infection due to multiple procedures, lead addition, and revisions and upgrade procedures.	M, O
The entirely S-ICD should be considered as an alternative to transvenous or epicardial approaches in the older child, patients with congenital heart disease, and those with limited or no venous access. Patients with a bradycardia indication, anti-tachycardia pacing, or cardiac resynchronization therapy requirements are not appropriate candidates.	O

Modified table from EHRA international consensus document on how to prevent, diagnose, and treat CIED infections.[20]
EHRA Statement classes; turquoise = recommended/indicated or 'should do this'; red = may be used or recommended; and green = should not be used or recommended.
EHRA ROME coding: R, randomized trials; O, observational studies; M, meta-analysis; E, expert opinion.
CIED, cardiac implantable electrical devices; LPM, leadless pacemaker; S-ICD, subcutaneous implantable defibrillator; *S. aureus, Staphylococcus aureus.*
*As defined in the WRAP-IT study population (ref 74) (patients undergoing pocket or lead revision, generator replacement, system upgrade, or an initial CRT-D implantation) and patients with other high risk factors, considering also the local incidence of CIED infections.

Glove change when draping the patient and before handling the generator may reduce risk for infection, although large-scale randomized clinical trials are lacking.[20] There is some support that bacterial glove contamination before handling the generator is common[66] and that double-gloving reduces the rate of inner glove perforation, but it is unclear whether microbial transmission and the rate of post-operative infectious complications are reduced. Non-powdered gloves may reduce the risk of infection by reducing local inflammation.[67]

Good surgical technique

Actions to avoid pocket haematoma. Special focus should be given to avoid pocket haematoma, particularly in patients with increased risk for bleeding.[68] Sub-pectoral pockets double the risk for pocket haematoma and should only be reserved for selected patients, such as those with low body mass.[68]

Adequate haemostasis by minimizing tissue damage and adequate wound closure are all important actions to reduce infection. Intraoperative administration of haemostatic agents has been suggested to give better haemostatis and less tissue damage, although there is little evidence to support such actions on a routine basis.[20,69,70] Pulsed electron avalanche knife, may potentially be beneficial compared with traditional electrocautery, in patients receiving antithrombotic therapy with respect to prevention of bleeding complications.[71]

Capsulectomy, excision of the fibrous capsule formed in the pocket, should not be performed routinely at re-interventions as it could result in more pocket bleeding/haematoma.[20,72] Moreover, pocket haematoma aspiration for diagnostic or therapeutic purpose is contraindicated given the risk of 'inoculating' the pocket and causing an infection (*Table 2*).[12,40] Haematoma evacuation should only be performed operatively in rare selected cases if pain is unmanageable or wound closure is threatened.[12,20,40] Vigorous pocket irrigation is important to remove devitalized tissue as well as dilute any contaminants.[73]

Pressure dressing may be used for the first 24 h to give better haemostatis, although there is little evidence to support it on a routine basis.[20]

Local intraoperative antibiotics or antiseptics

There is limited support for the use of *antiseptic or antibiotic pocket irrigation* as indicated by the PADIT trial[56] and is not recommended.[20]

Recommendation for an *antibacterial mesh envelope* (TYRX^{TM}, Medtronic, MN, USA) shown to significantly reduce major CIED infections in high-risk patients (WRAP-IT trial),[74,75] and be cost-effective[76] is discussed in more detail below (*Tables 1 and 2*).[20]

Closure of pocket

Closure in layers minimizes wound tension and reduces the risk of dehiscence and infection.[20,77] If skin closure is performed with non-absorbable material, it must be removed in a timely manner (usually 7–14 days) and if performed by absorbable sutures, they must be placed to allow for absorption and avoidance of a 'stitch abscess'. Whether the type of suture material impacts the risk of infection is unclear. The preventive effects of sutures impregnated with antibiotics are also unclear and they are therefore not recommended over standard sutures.[20] Abdominal pocket should not be used as it is associated with a four-fold risk for infection.[15]

Procedure-related preventive actions are described in *Tables 1 and 2*.

Post-procedural actions

Post-procedure antibiotic therapy is not recommended[20] given the results of the PADIT trial, showing no benefit of incremental perioperative antibiotics using preprocedural cefazolin and vancomycin, intraoperative bacitracin pocket wash and 2-day postoperative oral cephalexin.[56]

Wound care, such as changing the dressing, is not recommended unless it becomes impregnated. Patients should be advised to avoid soaking the wound until it is entirely healed after approximately a month.[20]

Staff training, physician skill, centre volume, and patient education

All personnel involved in CIED implantations must have the required competence and skills for strict sterile techniques and behaviour in operating room settings including scrubbing, setting up tables, patient preparation, and strict limitation of operating room traffic. They should further be aware of all risk factors for complications and infections so that preventive actions can be made.

Short procedure times should be secured by ensuring adequate equipment, room facilities, well-trained staff, and operators with access to supervisors since long procedure time has been associated with infectious complications (85 vs. 60 min)[14,15] and was shown to increase the risk of infection stepwise as compared to durations shorter than 30 min, with increases 1.5 times for durations 60–90 min and 2.4 times for those exceeding 120 min.[11] Inexperienced operator, in particular thoracic surgeon, was associated with an almost three-fold risk for device infection,[78] and was shown to be an independent risk factor for any complication (adjusted risk ratio of 1.9, 95% confidence interval 1.4–2.6) if the annual volume was <50 procedures.[9] The higher infection rates observed for CRT devices[28] and the nearly six-fold higher infection risk for CRT-Ds vs. CRT-Ps, underlines the need for adequately trained operators,[7,9,10,14,15,33,49,50,57] and the need for supervision for each type of device implant procedure.[79]

Patients should be educated about the risks and signs of infection and instructed to seek medical attention in case of signs of infection.

Higher complication rates and higher risks for CIED infections have been observed for centres with <750 device implantations annually,[9] whereas others reported that high-volume centres (>200 per year) were protected against device infections, observations that emphasize the importance of securing adequate implantation volumes annually at the hospital level.[80]

Environmental, organizational, and surveillance actions

Standards for sterile procedures in operating rooms and Electrophysiology/Catheterization laboratories must be met as for other surgical procedures associated with implants.[81] This includes standards for cleaning, room design, presence of proper ventilation system with positive pressure in operating rooms, optimization of air

quality with filtered air and frequent air exchanges, restricting area traffic and access to the operating room during working hours. 'Out-of-hours procedures' must be avoided as it increases the risk for infection by 1.5.[9]

Existing *surveillance structures* for CIED infections are lacking in many institutions. A continuous surveillance program for recording of procedure-related complication- and infection rates and flora involved should be in place in all centres performing implantations in order to increase awareness, reduce reluctance of reporting complications and give incentive for preventive measures. The registration must include clinical data on the individual patient, procedure, staff and device implanted including all reoperations. Since device complication rates are frequently underreported in registries, with threefold lower reported total major complication rates as compared with randomized trials,[82] cross checking of data is encouraged to minimize risk of both underreporting and misclassification of events. A semi-automated detection algorithm based on diagnosis codes and structured electronic medical records for identifying device infections may potentially be a useful tool for surveillance of CIED infections with feedback to clinicians.[83] A similar algorithm, based on structured and free text diagnostic—therapeutic data using electronic medical records, was constructed to more reliably and efficiently measure CIED infections, and resulted in a positive predictive value of 43.5% with an overall sensitivity and specificity of 94.4% and 48.8%, respectively.[84]

Conclusions

The continued rise in device-related infections, particularly in CRT recipients and patients with high comorbidity burden, highlights the need for novel and more extensive preventive strategies to stop this development.

A greater awareness and improved actions to prevent device infections may be achieved by a comprehensive effective surveillance of infections on centre level collecting data on procedures, treatments, outcomes, and costs. Such registries should be user-friendly and standardized, and apart from device infections also focus on procedure-related complications. Educational activities focusing on preventive actions with tools for better implementation of guidelines, targeting not only physicians but also patients, are also needed. While preventive actions are exceedingly important, monitoring risks, and acknowledging them may be even more challenging.

Funding

This article was published as part of a supplement supported by an educational grant from Medtronic.

Conflict of interest: C.B.-L. declares direct personal payment from Bayer, Sanofi Aventis, MSD, Medtronic, Cathprint, Pfizer, Johnson-Johnson, Phillips, and Boston Sci. B.O. has nothing to disclose.

References

1. Greenspon AJ, Patel JD, Lau E, Ochoa JA, Frisch DR, Ho RT *et al.* 16-Year trends in the infection burden for pacemakers and implantable cardioverter-defibrillators in the United States 1993 to 2008. *J Am Coll Cardiol* 2011;**58**:1001–6.
2. Le KY, Sohail MR, Friedman PA, Uslan DZ, Cha SS, Hayes DL *et al.*; Mayo Cardiovascular Infections Study Group. Clinical predictors of cardiovascular implantable electronic device-related infective endocarditis. *Pacing Clin Electrophysiol* 2011;**34**:450–9.
3. Sohail MR, Henrikson CA, Braid-Forbes MJ, Forbes KF, Lerner DJ. Mortality and cost associated with cardiovascular implantable electronic device infections. *Arch Intern Med* 2011;**171**:1821–8.
4. Tarakji KG, Chan EJ, Cantillon DJ, Doonan AL, Hu T, Schmitt S *et al.* Cardiac implantable electronic device infections: presentation, management, and patient outcomes. *Heart Rhythm* 2010;**7**:1043–7.
5. Habib A, Le KY, Baddour LM, Friedman PA, Hayes DL, Lohse CM *et al.*; Mayo Cardiovascular Infections Study Group. Predictors of mortality in patients with cardiovascular implantable electronic device infections. *Am J Cardiol* 2013;**111**:874–9.
6. Rennert-May E, Chew D, Lu S, Chu A, Kuriachan V, Somayaji R. Epidemiology of cardiac implantable electronic device infections in the United States: a population-based cohort study. *Heart Rhythm* 2020;**17**:1125–31.
7. Joy PS, Kumar G, Poole JE, London B, Olshansky B. Cardiac implantable electronic device infections: who is at greatest risk? *Heart Rhythm* 2017;**14**:839–45.
8. Voigt A, Shalaby A, Saba S. Continued rise in rates of cardiovascular implantable electronic device infections in the United States: temporal trends and causative insights. *Pacing Clin Electrophysiol* 2010;**33**:414–9.
9. Kirkfeldt RE, Johansen JB, Nohr EA, Jorgensen OD, Nielsen JC. Complications after cardiac implantable electronic device implantations: an analysis of a complete, nationwide cohort in Denmark. *Eur Heart J* 2014;**35**:1186–94.
10. Barra S, Providência R, Boveda S, Duehmke R, Narayanan K, Chow AW *et al.* Device complications with addition of defibrillation to cardiac resynchronisation therapy for primary prevention. *Heart* 2018;**104**:1529–35.
11. Olsen T, Jørgensen OD, Nielsen JC, Thøgersen AM, Philbert BT, Johansen JB. Incidence of device-related infection in 97 750 patients: clinical data from the complete Danish device-cohort (1982–2018). *Eur Heart J* 2019;**40**:1862–9.
12. Klug D, Balde M, Pavin D, Hidden-Lucet F, Clementy J, Sadoul N *et al.*; PEOPLE Study Group. Risk factors related to infections of implanted pacemakers and cardioverter-defibrillators: results of a large prospective study. *Circulation* 2007;**116**:1349–55.
13. Poole JE, Gleva MJ, Mela T, Chung MK, Uslan DZ, Borge R *et al.*; REPLACE Registry Investigators. Complication rates associated with pacemaker or implantable cardioverter-defibrillator generator replacements and upgrade procedures: results from the REPLACE registry. *Circulation* 2010;**122**:1553–61.
14. Romeyer-Bouchard C, Da Costa A, Dauphinot V, Messier M, Bisch L, Samuel B *et al.* Prevalence and risk factors related to infections of cardiac resynchronization therapy devices. *Eur Heart J* 2010;**31**:203–10.
15. Polyzos KA, Konstantelias AA, Falagas ME. Risk factors for cardiac implantable electronic device infection: a systematic review and meta-analysis. *Europace* 2015;**17**:767–77.
16. Jędrzejczyk-Patej E, Mazurek M, Kowalski O, Sokal A, Kozieł M, Adamczyk K *et al.* Device-related infective endocarditis in cardiac resynchronization therapy recipients; single center registry with over 2500 person-years follow up. *Int J Cardiol* 2017;**227**:18–24.
17. Kusumoto FM, Schoenfeld MH, Wilkoff BL, Berul CI, Birgersdotter-Green UM, Carrillo R *et al.* 2017 HRS expert consensus statement on cardiovascular implantable electronic device lead management and extraction. *Heart Rhythm* 2017;**14**:e503–51.
18. Sandoe JA, Barlow G, Chambers JB, Gammage M, Guleri A, Howard P *et al.*; British Society for Echocardiography. Guidelines for the diagnosis, prevention and management of implantable cardiac electronic device infection. Report of a joint Working Party project on behalf of the British Society for Antimicrobial Chemotherapy (BSAC, host organization), British Heart Rhythm Society (BHRS), British Cardiovascular Society (BCS), British Heart Valve Society (BHVS) and British Society for Echocardiography (BSE). *J Antimicrob Chemother* 2015;**70**:325–59.
19. Habib G, Lancellotti P, Antunes MJ, Bongiorni MG, Casalta JP, Del Zotti F *et al.*; ESC Scientific Document Group. 2015 ESC Guidelines for the management of infective endocarditis: the Task Force for the Management of Infective Endocarditis of the European Society of Cardiology (ESC). Endorsed by: European Association for Cardio-Thoracic Surgery (EACTS), the European Association of Nuclear Medicine (EANM). *Eur Heart J* 2015;**36**:3075–128.
20. Blomström-Lundqvist C, Traykov V, Erba PA, Burri H, Nielsen JC, Bongiorni MG *et al.*; ESC Scientific Document Group. European Heart Rhythm Association (EHRA) international consensus document on how to prevent, diagnose, and treat cardiac implantable electronic device infections—endorsed by the Heart Rhythm Society (HRS), the Asia Pacific Heart Rhythm Society (APHRS), the Latin American Heart Rhythm Society (LAHRS), International Society for Cardiovascular Infectious Diseases (ISCVID) and the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS). *Europace* 2020;**22**:515–49.

21. Traykov V, Bongiorni MG, Boriani G, Burri H, Costa R, (LAHRS representative), Dagres N, *et al.* Clinical practice and implementation of guidelines for the prevention, diagnosis and management of cardiac implantable electronic device infections; results of a worldwide survey under the auspices of the European Heart Rhythm Association. *Europace* 2019;**21**:1270–9.
22. Rao A, Garner D, Starck C, Kirkfeldt RE, Dagres N, Didier K *et al.* Knowledge gaps, lack of confidence, and system barriers to guideline implementation among European physicians managing patients with CIED lead or infection complications: a European Heart Rhythm Association/European Society of Cardiology educational needs assessment survey. *Europace* 2020;**22**:1743–53.
23. Nagpal A, Baddour LM, Sohail MR. Microbiology and pathogenesis of cardiovascular implantable electronic device infections. *Circ Arrhythm Electrophysiol* 2012;**5**: 433–41.
24. Ludwig S, Theis C, Wolff C, Nicolle E, Witthohn A, Götte A. Complications and associated healthcare costs of transvenous cardiac pacemakers in Germany. *J Comp Eff Res* 2019;**8**:589–97.
25. de Vries FE, Gans SL, Solomkin JS, Allegranzi B, Egger M, Dellinger EP *et al.* Meta-analysis of lower perioperative blood glucose target levels for reduction of surgical-site infection. *Br J Surg* 2017;**104**:e95–e105.
26. Maille B, Koutbi L, Resseguier N, Lemoine C, Thuny F, Peyrol M *et al.* Seasonal variations in cardiac implantable electronic device infections. *Heart Vessels* 2019; **34**:824–31.
27. Da Costa A, Lelièvre H, Kirkorian G, Célard M, Chevalier P, Vandenesch F *et al.* Role of the preaxillary flora in pacemaker infections. *Circulation* 1998;**97**:1791–5.
28. Palmisano P, Accogli M, Zaccaria M, Luzzi G, Nacci F, Anaclerio M *et al.* Rate, causes, and impact on patient outcome of implantable device complications requiring surgical revision: large population survey from two centres in Italy. *Europace* 2013;**15**:531–40.
29. Hussein AA, Baghdy Y, Wazni OM, Brunner MP, Kabbach G, Shao M *et al.* Microbiology of cardiac implantable electronic device infections. *JACC Clin Electrophysiol* 2016;**2**:498–505.
30. Harper MW, Uslan DZ, Greenspon AJ, Baddour LM, Carrillo RG, Danik SB *et al.* Clinical presentation of CIED infection following initial implant versus reoperation for generator change or lead addition. *Open Heart* 2018;**5**:e000681.
31. Uslan DZ, Sohail MR, St SJ, Friedman PA, Hayes DL, Stoner SM *et al.* Permanent pacemaker and implantable cardioverter defibrillator infection: a population-based study. *Arch Intern Med* 2007;**167**:669–75.
32. Sohail MR, Uslan DZ, Khan AH, Friedman PA, Hayes DL, Wilson WR *et al.* Management and outcome of permanent pacemaker and implantable cardioverter-defibrillator infections. *J Am Coll Cardiol* 2007;**49**:1851–9.
33. Koneru JN, Jones PW, Hammill EF, Wold N, Ellenbogen KA. Risk factors and temporal trends of complications associated with transvenous implantable cardiac defibrillator leads. *JAHA* 2018;**7**:e007691.
34. Kumar DS, Tompkins CM, Veenhuyzen GD, Henrikson CA. Significance of leukocytosis prior to cardiac device implantation. *Pacing Clin Electrophysiol* 2018;**41**: 1197–200.
35. El-Chami MF, Soejima K, Piccini JP, Reynolds D, Ritter P, Okabe T *et al.* Incidence and outcomes of systemic infections in patients with leadless pacemakers: data from the Micra IDE study. *Pacing Clin Electrophysiol* 2019;1105–10. [Epub ahead of print].
36. El-Chami MF, Clementy N, Garweg C, Omar R, Duray GZ, Gornick CC *et al.* Leadless pacemaker implantation in hemodialysis patients: experience with the micra transcatheter pacemaker. *JACC Clin Electrophysiol* 2019;**5**:162–70.
37. Knops RE, Olde Nordkamp LRA, Delnoy PHM, Boersma LVA, Kuschyk J, El-Chami MF, PRAETORIAN Investigators *et al.* Subcutaneous or transvenous defibrillator therapy. *N Engl J Med* 2020;**383**:526–36.
38. Viani S, Migliore F, Tola G, Pisanò ECL, Russo AD, Luzzi G *et al.* Use and outcomes of subcutaneous implantable cardioverter-defibrillator (ICD) after transvenous ICD extraction: an analysis of current clinical practice and a comparison with transvenous ICD reimplantation. *Heart Rhythm* 2019;**16**:564–71.
39. Asif A, Carrillo R, Garisto J-D, Lopera G, Ladino M, Barakat U *et al.* Epicardial cardiac rhythm devices for dialysis patients: minimizing the risk of infection and preserving central veins. *Semin Dial* 2012;**25**:88–94.
40. Essebag V, Verma A, Healey JS, Krahn AD, Kalfon E, Coutu B *et al.* Clinically significant pocket hematoma increases long-term risk of device infection: BRUISE CONTROL INFECTION Study. *J Am Coll Cardiol* 2016;**67**:1300–8.
41. Birnie DH, Healey JS, Wells GA, Verma A, Tang AS, Krahn AD *et al.* Pacemaker or defibrillator surgery without interruption of anticoagulation. *N Engl J Med* 2013;**368**:2084–93.
42. Birnie DH, Healey JS, Wells GA, Ayala-Paredes F, Coutu B, Sumner GL *et al.* Continued vs. interrupted direct oral anticoagulants at the time of device surgery, in patients with moderate to high risk of arterial thrombo-embolic events (BRUISE CONTROL-2). *Eur Heart J* 2018;**39**:3973–9.
43. Essebag V, Healey JS, Joza J, Nery PB, Kalfon E, Leiria TLL *et al.* Effect of direct oral anticoagulants, warfarin, and antiplatelet agents on risk of device pocket hematoma: combined analysis of BRUISE CONTROL 1 and 2. *Circ Arrhythm Electrophysiol* 2019;**12**:e007545.
44. Robinson M, Healey JS, Eikelboom J, Schulman SAM, Morillo CA, Nair GM *et al.* Postoperative low-molecular-weight heparin bridging is associated with an increase in wound hematoma following surgery for pacemakers and implantable defibrillators. *Pacing Clin Electrophysiol* 2009;**32**:378–82.
45. Du L, Zhang Y, Wang W, Hou Y. Perioperative anticoagulation management in patients on chronic oral anticoagulant therapy undergoing cardiac devices implantation: a meta-analysis. *Pacing Clin Electrophysiol* 2014;**37**:1573–86.
46. Kutinsky IB, Jarandilla R, Jewett M, Haines David E. Risk of hematoma complications after device implant in the clopidogrel era. *Circ Arrhythm Electrophysiol* 2010; **3**:312–8.
47. Pokorney SD, Mi X, Lewis RK, Greiner M, Epstein LM, Carrillo RG *et al.* Outcomes associated with extraction versus capping and abandoning pacing and defibrillator leads. *Circulation* 2017;**136**:1387–95.
48. Hussein AA, Tarakji KG, Martin DO, Gadre A, Fraser T, Kim A *et al.* Cardiac implantable electronic device infections: added complexity and suboptimal outcomes with previously abandoned leads. *JACC Clin Electrophysiol* 2017;**3**:1–9.
49. Nery P, Fernandes R, Nair G, Sumner GL, Ribas C, Menon S *et al.* Device-related infection among patients with pacemakers and implantable defibrillators: incidence, risk factors, and consequences. *J Cardiovasc Electrophysiol* 2010;**21**:786–90.
50. Mittal S, Shaw RE, Michel K, Palekar R, Arshad A, Musat D *et al.* Cardiac implantable electronic device infections: incidence, risk factors, and the effect of the AigisRx antibacterial envelope. *Heart Rhythm* 2014;**11**:595–601.
51. Bode LGM, Kluytmans JAJW, Wertheim HFL, Bogaers D, Vandenbroucke-Grauls CMJE, Roosendaal R *et al.* Preventing surgical-site infections in nasal carriers of *Staphylococcus aureus*. *N Engl J Med* 2010;**362**:9–17.
52. Franco LM, Cota GF, Pinto TS, Ercole FF. Preoperative bathing of the surgical site with chlorhexidine for infection prevention: systematic review with meta-analysis. *Am J Infect Control* 2017;**45**:343–9.
53. Cai Y, Xu K, Hou W, Yang Z, Xu P. Preoperative chlorhexidine reduces the incidence of surgical site infections in total knee and hip arthroplasty: a systematic review and meta-analysis. *Int J Surg* 2017;**39**:221–8.
54. de Oliveira JC, Martinelli M, Nishioka SADO, Varejao T, Uipe D, Pedrosa AAA *et al.* Efficacy of antibiotic prophylaxis before the implantation of pacemakers and cardioverter-defibrillators: results of a large, prospective, randomized, double-blinded, placebo-controlled trial. *Circ Arrhythm Electrophysiol* 2009;**2**:29–34.
55. Da Costa A, Kirkorian G, Cucherat M, Delahaye F, Chevalier P, Cerisier A *et al.* Antibiotic prophylaxis for permanent pacemaker implantation: a meta-analysis. *Circulation* 1998;**97**:1796–801.
56. Krahn AD, Longtin Y, Philippon F, Birnie DH, Manlucu J, Angaran P *et al.* Prevention of arrhythmia device infection trial: the PADIT Trial. *J Am Coll Cardiol* 2018;**72**:3098–109.
57. Prutkin JM, Reynolds MR, Bao H, Curtis JP, Al-Khatib SM, Aggarwal S *et al.* Rates of and factors associated with infection in 200 909 Medicare implantable cardioverter-defibrillator implants: results from the National Cardiovascular Data Registry. *Circulation* 2014;**130**:1037–43.
58. Shariff N, Akthar T, Razak E, Segerson N, Schwartzman D. Cardiovascular implantable electronic device infections: risk scoring and role of antibiotic envelope in prevention. *Recent Adv Cardiovasc Drug Discov* 2015;**10**:70–6.
59. Balla C, Brieda A, Righetto A, Vitali F, Malagù M, Cultrera R *et al.* Predictors of infection after "de novo" cardiac electronic device implantation. *Eur J Intern Med* 2020;**77**:73–8.
60. Birnie DH, Wang J, Alings M, Philippon F, Parkash R, Manlucu J *et al.* Risk factors for infections involving cardiac implanted electronic devices. *J Am Coll Cardiol* 2019;**74**:2845–54.
61. Ahmed F, Blomström-Lundqvist C, Bloom H, Cooper C, Ellis C, Goette A *et al.* Use of healthcare claims to validate the PADIT CIED infection risk score. *Europace* 2021.
62. Darouiche RO, Wall MJ Jr, Itani KM, Otterson MF, Webb AL, Carrick MM *et al.* Chlorhexidine-alcohol versus povidone-iodine for surgical-site antisepsis. *N Engl J Med* 2010;**362**:18–26.
63. Mimoz O, Lucet JC, Kerforne T, Pascal J, Souweine B, Goudet V *et al.* Skin antisepsis with chlorhexidine-alcohol versus povidone iodine-alcohol, with and without skin scrubbing, for prevention of intravascular-catheter-related infection (CLEAN): an open-label, multicentre, randomised, controlled, two-by-two factorial trial. *Lancet* 2015;**386**:2069–77.
64. Mohammed Q, Omeed Z, Muhammad H, Amy H, Oussama W, L WB *et al.* The Impact of changing antiseptic skin preparation agent used for cardiac implantable electronic device (CIED) procedures on the risk of infection. *Pacing Clin Electrophysiol* 2015;**38**:240–6.
65. Webster J, Alghamdi A. Use of plastic adhesive drapes during surgery for preventing surgical site infection. *Cochrane Database Syst Rev* 2015;**4**:CD006353.
66. Kozon I, Riahi S, Lundbye-Christensen S, Thøgersen AM, Ejlertsen T, Aaen D *et al.* Risk factors of cardiac device infection: glove contamination during device procedures. *Am J Infect Control* 2017;**45**:866–71.

67. Suding P, Nguyen T, Gordon I, Wilson SE. Glove powder increases *Staphylococcus aureus* abscess rate in a rat model. *Surg Infect (Larchmt)* 2010;**11**:133–5.
68. Masiero S, Connolly SJ, Birnie D, Neuzner J, Hohnloser SH, Vinolas X *et al.* Wound haematoma following defibrillator implantation: incidence and predictors in the Shockless Implant Evaluation (SIMPLE) trial. *Europace* 2017;**19**:1002–6.
69. Tscholl V, Spann F, Moses J, Nagel P, Bellmann B, Biewener S *et al.* Prospective randomized study evaluating the effects of PerClot® (Polysaccharide Hemostatic System) application in patients with high bleeding risk undergoing cardiac rhythm device implantation. *Int J Cardiol* 2017;**248**:84–91.
70. Ohlow MA, Lauer B, Buchter B, Schreiber M, Geller JC. Pocket related complications in 163 patients receiving anticoagulation or dual antiplatelet therapy: D-Stat Hemostat versus standard of care. *Int J Cardiol* 2012;**159**:177–80.
71. Kaya E, Siebermair J, Azizy O, Dobrev D, Rassaf T, Wakili R. Use of pulsed electron avalanche knife (PEAK) PlasmaBlade™ in patients undergoing implantation of subcutaneous implantable cardioverter-defibrillator. *Int J Cardiol Heart Vasc* 2019;**24**:100390.
72. Lakkireddy D, Pillarisetti J, Atkins D, Biria M, Reddy M, Murray C *et al.* IMpact of pocKet rEvision on the rate of InfecTion and other CompLications in patients rEquiring pocket mAnipulation for generator replacement and/or lead replacement or revisioN (MAKE IT CLEAN): a prospective randomized study. *Heart Rhythm* 2015;**12**:950–6.
73. NICE Guideline Updates Team. *Surgical Site Infections: Prevention and Treatment. NICE Guideline No 125*. London, UK: National Institute for Health and Care Excellence; 2019.
74. Tarakji KG, Mittal S, Kennergren C, Corey R, Poole JE, Schloss E *et al.* Antibacterial envelope to prevent cardiac implantable device infection. *N Engl J Med* 2019;**380**:1895–905.
75. Kumar A, Doshi R, Shariff M. Role of antibiotic envelopes in preventing cardiac implantable electronic device infection: A meta-analysis of 14 859 procedures. *J Arrhythmia* 2020;**36**:176–9.
76. Wilkoff BL, Boriani G, Mittal S, Poole JE, Kennergren C, Corey GR *et al.* Cost-effectiveness of an antibacterial envelope for cardiac implantable electronic device infection prevention in the US Healthcare System from the WRAP-IT Trial. *Circ Arrhythm Electrophysiol* 2020;**13**:e008503.
77. Grubb B, Welch M, Karabin B, Foster W, Zhang D, Kanjwal K. Initial experience with a technique for wound closure after cardiac device implantation designed to reduce infection and minimize tissue scar formation. *Am J Ther* 2012;**19**:88–91.
78. Al-Khatib SM, Greiner MA, Peterson ED, Hernandez AF, Schulman KA, Curtis LH. Patient and implanting physician factors associated with mortality and complications after implantable cardioverter-defibrillator implantation, 2002-2005. *Circ Arrhythm Electrophysiol* 2008;**1**:240–9.
79. Merino JL, Arribas F, Botto GL, Huikuri H, Kraemer LI, Linde C *et al.* Core curriculum for the heart rhythm specialist. *Europace* 2009;**11**:1–26.
80. Lin Y-S, Hung S-P, Chen P-R, Yang C-H, Wo H-T, Chang P-C *et al.* Risk factors influencing complications of cardiac implantable electronic device implantation: infection, pneumothorax and heart perforation: a nationwide population-based cohort study. *Medicine (Baltimore)* 2014;**93**:e213.
81. Haines DE, Beheiry S, Akar JG, Baker JL, Beinborn D, Beshai JF *et al.* Heart Rhythm Society Expert Consensus Statement on electrophysiology laboratory standards: process. *Heart Rhythm* 2014;**11**:e9–e51.
82. Ezzat VA, Lee V, Ahsan S, Chow AW, Segal O, Rowland E *et al.* A systematic review of ICD complications in randomised controlled trials versus registries: is our 'real-world' data an underestimation? *Open Heart* 2015;**2**:e000198.
83. Asundi A, Stanislawski M, Mehta P, Mull HJ, Schweizer ML, Barón AE *et al.* Development and validation of a semi-automated surveillance algorithm for cardiac device infections: insights from the VA CART program. *Sci Rep* 2020;**10**:5276.
84. Mull HJ, Stolzmann KL, Shin MH, Kalver E, Schweizer ML, Branch-Elliman W. Novel method to flag cardiac implantable device infections by integrating text mining with structured data in the veterans health administration's electronic medical record. *JAMA Netw Open* 2020;**3**:e2012264.